IN THE UNITED STATES DISTRICT COURT FOR THE DISTRICT OF UTAH

CENTRAL DIVISION

PHARMANEX, INC., a Delaware corporation authorized to do business in the State of Utah,

Plaintiff,

vs.

DONNA SHALALA, in her official capacity as Secretary of the United States Department of Health and Human Services, and JANE E. HENNEY, in her official capacity as First Deputy Commissioner of the Food and Drug Administration,

Defendants.

MEMORANDUM DECISION AND ORDER

Case No. 2:97CV262K

This matter is before the court on remand from the Tenth Circuit Court of Appeals. Previously, Defendants ("FDA") had filed a Motion to Affirm Administrative Decision, and Plaintiff ("Pharmanex") had filed a Motion to Hold Unlawful and Set Aside FDA's Decision of May 20, 1998. In February 1998, this court granted Pharmanex's motion and set aside FDA's determination that Pharmanex's product, Cholestin, was a drug. This court found that Cholestin is a "dietary supplement" within the definition set forth in 21 U.S.C. § 321(ff), based on the determination that § 321(ff)(3)(B) refers unambiguously to finished drug products, rather than their individual constituents. Because of that ruling, it was unnecessary to reach the other issues

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raised by the parties. In July 2000, the Tenth Circuit reversed this court's decision, finding that section 321(ff)(3)(B) is sufficiently ambiguous to merit *Chevron* deference and that FDA's interpretation of § 321(ff)(3)(B) is not arbitrary, capricious, or manifestly contrary to the statute. Thus, the active ingredients of approved new drugs, such as lovastatin, could be articles that are approved as new drugs and, as such, are excluded from the definition of dietary supplement under § 321(ff)(3). Consequently, the Tenth Circuit remanded the case for consideration of the record-based issues not previously reached by this court..

Accordingly, the court instructed the parties to brief the issues that remained in the case.[1] A hearing on the remaining issues was held on December 22, 2000. At the hearing, Pharmanex was represented by Richard M. Cooper, and FDA was represented by Drake Cutini. Before the hearing, the court considered carefully the memoranda and other materials submitted by the parties. Since taking the matter under advisement, the court has further considered the law and facts relating to this motion. Now being fully advised, the court renders the following Memorandum Decision and Order.

I. BACKGROUND

The background of Pharmanex's product, Cholestin, and the history of the administrative proceedings and the subsequent litigation involving FDA's decision that Cholestin is a drug, is set forth in the Tenth Circuit's decision and need not be repeated here. *See Pharmanex v.*

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[1] In response, Pharmanex filed a new Motion to Hold Unlawful and Set Aside the Food and Drug Administration's Decision of May 20, 1998 and an accompanying memorandum in support. FDA's briefing is captioned as "Government's Supplemental Memorandum," and is in further support of its previous Motion to Affirm Administrative Decision.

Shalala, 221 F.3d 1151 (10th Cir. 2000).

The parties agree that the remaining issues on remand are the following: whether FDA was arbitrary and capricious in determining (1) that Pharmanex, in manufacturing and marketing Cholestin, was actually manufacturing and marketing lovastatin; and (2) that lovastatin had not been "marketed as a dietary supplement or as a food" prior to its approval as a "new drug."[2]

The relevant statutory provision regarding these two issues is the exclusionary clause found at 21 U.S.C. § 321(ff)(3)(B), which provides in pertinent part that the term "dietary supplement":

> "(B) [does not include] an article that is approved as a new drug under Section 355 of this title [21 U.S.C. § 355] . . . which was not before such approval . . . marketed as a dietary supplement or as a food . . . ."

21 U.S.C. § 321(ff)(3)(B). In its Decision, FDA determined that Cholestin is excluded from the definition of dietary supplement under § 321(ff)(3) because it includes an article, lovastatin, which was approved as a new drug under 21 U.S.C. § 355 and because lovastatin was not "marketed as a dietary supplement or as a food" before FDA approved lovastatin as a new drug in 1987.

FDA determined that the relevant "article" for purposes of § 321(ff)(3) is lovastatin based on evidence that (1) Pharmanex manufactures Cholestin in a manner designed to ensure that the product contains significant amounts of lovastatin, and (2) Pharmanex promotes Cholestin for its lovastatin content.

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[2] As discussed below, Pharmanex does not agree that the second issue (regarding the prior market clause) is controlled by an arbitrary and capricious standard of review. *See* footnote 5, *infra*.

II. STANDARD OF REVIEW

Because the issues before this court involve the factual determinations made by the agency and FDA's application of those facts to reach specific conclusions, this court's review is governed by the Administrative Procedures Act ("APA"), which authorizes the court to set aside FDA's Decision only if it finds that the Decision is arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law. 5 U.S.C. § 706(2)(A). An agency's factual determinations comply with the APA if based upon such relevant evidence as a reasonable mind might accept as adequate to support a conclusion. *Dickinson v. Zurko*, 527 U.S. 150, 162 (1999). "Evidence is substantial in the APA sense if is enough to justify, if the trial were to a jury, a refusal to direct a verdict when the conclusion to be drawn is one of fact." *Olenhouse v. Commodity Credit Corp.*, 42 F.3d 1560, 1575 (10th Cir. 1994). Thus,

> the court must consider whether the decision was based on a consideration of the relevant factors and whether there has been a clear error of judgment. Although this inquiry into the facts is to be searching and careful, the ultimate standard of review is a narrow one. This court is not empowered to substitute its judgment for that of the agency.

Citizens to Preserve Overton Park, Inc. v. Volpe, 401 U.S. 402, 416 (1971) (citations omitted).

In reviewing agency action under the APA, the court must also determine whether there has been a "clear error of judgment." *Id.*; *Olenhouse*, 42 F.3d at 1574. In determining whether there has been a "clear error of judgment," the court must ascertain whether FDA has articulated a "rational connection between the facts found and the decision made." *Motor Vehicle Mfrs. Ass'n v. Stat Farm Mut. Ins. Co.*, 463 U.S. 29, 43 (1983) (quotations and citation omitted); *Olenhouse*, 42 F.3d at 1574.

III. DISCUSSION

A. ANALYSIS OF FDA'S DETERMINATION THAT THE RELEVANT "ARTICLE" FOR PURPOSES OF § 321(FF)(3)(B) IS LOVASTATIN BECAUSE PHARMANEX, IN MANUFACTURING AND MARKETING CHOLESTIN, IS MANUFACTURING AND MARKETING LOVASTATIN

1. Pharmanex's Arguments

Pharmanex argues that FDA's determination that the relevant "article" for purposes of § 321(ff)(3)(B) is lovastatin is arbitrary and capricious. It contends that its manufacturing practices do not emphasize Cholestin's lovastatin content and that its marketing practices do not promote the presence of lovastatin in Cholestin. Specifically, Pharmanex argues that the administrative record does not support FDA's factual determinations that traditional red yeast rice does not contain lovastatin, that Pharmanex's use of one specific strain of red yeast fungus supports the conclusion that it is manufacturing lovastatin, that it controls temperatures to ensure production of lovastatin during the manufacture of Cholestin, that Pharmanex's tracking of the levels of HMG-CoA reductase inhibitors is a surrogate for monitoring the total quantity of lovastatin in the red yeast rice, and that Pharmanex markets lovastatin. It claims that FDA's determinations are arbitrary and capricious because the evidence does not support the conclusions and because FDA ignored material evidence.

Pharmanex argues that the only fair conclusion, based upon the record and according to the standards established by FDA, is that the relevant "article" is the dietary ingredient contained in Cholestin, known as red yeast rice. Because red yeast rice is the relevant article, then the "article" was never in fact approved by FDA as a new drug, and marketing Cholestin as a dietary supplement is lawful and completely consistent with the Dietary Supplement Health and

Education Act.[3]

2. FDA's Arguments

FDA argues that its determination that Pharmanex, in manufacturing and marketing Cholestin,is manufacturing and marketing lovastatin is fully supported by the record. FDA cites to significant evidence that Pharmanex is manufacturing lovastatin, not traditional red yeast rice. Among other things, it points to several studies that demonstrate that traditional red yeast rice does not contain significant amounts of lovastatin, whereas Cholestin does. It points to evidence that Pharmanex's manufacturing processes produce a high amount of lovastatin and that, if Pharmanex's production processes were really not materially different that the traditional process for making red yeast rice, it would not have applied for a patent for an improved red yeast rice product that, Pharmanex asserted, was unlike traditional red yeast rice with respect to the lovastatin content and its use to treat high cholesterol. In addition, FDA argues that its determination that Pharmanex, in marketing Cholestin, was marketing lovastatin, is not arbitrary and capricious, pointing to significant evidence in the record.

3. Analysis

While Pharmanex adamantly contends that Cholestin is a "traditional" Asian product known alternatively as "red yeast rice," "Hong Qu," or "Red Koji," FDA concluded that Cholestin is not traditional red yeast rice. Significantly, FDA determined that traditional red

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[3] Pharmanex has provided arguments based on "new information" that has surfaced since this court last considered FDA's actions. To the extent that the new information contains factual material, it cannot be considered by the court because it was not part of the administrative record. However, even considering the new information provided by Pharmanex, the court's conclusions below are not altered.

yeast rice does not contain lovastatin, that Cholestin contains lovastatin, and that Cholestin is a carefully manufactured, non-traditional product designed to contain specific levels of lovastatin, the active ingredient of the approved prescription drug Mevacor, which is intended to reduce cholesterol and treat heart disease.

Specifically, FDA found that, unlike the manufacturing method for traditional red yeast rice, Pharmanex, when manufacturing Cholestin, deliberately selects and uses one specific strain of red yeast fungus, *Monascus purpureus* Went, intended to produce lovastatin. In addition, FDA concluded that Pharmanex controls temperatures to ensure production of lovastatin during the manufacture of Cholestin and that Pharmanex tracks the levels of HMG-CoA reductase inhibitors, which insures significant levels of lovastatin. Finally, FDA also concluded that Pharmanex promotes the lovastatin content of Cholestin.

Pharmanex has skillfully raised a variety of arguments as to why FDA's determination that Pharmanex is manufacturing and marketing lovastatin, not traditional red yeast rice, is not supported by the record. However, this court, after reviewing the briefs submitted by the parties (both prior to the appeal and after remand), listening to argument of counsel, reviewing the FDA Decision and the evidence in the administrative record, disagrees. In light of the standard of review applied to FDA's factual determinations this court cannot conclude that FDA's factual findings on this issue were arbitrary and capricious. Rather, there is evidence in the record that a reasonable mind might accept as adequate to support FDA's conclusion. *See Olenhouse*, 42 F.3d at 1575. There has been no clear error of judgment, as FDA has articulated "a rational connection between the facts found and the decision made." *See Motor Vehicle Mfrs. Ass'n v.*

State Farm Mut. Ins. Co., 463 U.S. at 43. Accordingly, the court affirms FDA's determination that the relevant "article" for purposes of § 321(ff)(3)(B) is lovastatin because Pharmanex, in manufacturing and marketing Cholestin, is manufacturing and marketing lovastatin.[4]

B. Analysis of FDA's Decision That Lovastatin Was Not Marketed As a Dietary Supplement or As a Food Prior to 1987

1. Pharmanex's Arguments

Pharmanex claims that, even if the relevant article is lovastatin, it was "marketed as a dietary supplement or as a food" prior to its approval as a new drug, and thus qualifies as a dietary supplement. Pharmanex argues that lovastatin was present in red rice yeast, oyster mushrooms, and other foods that were marketed in the United States and East Asia before lovastatin was approved as a new drug in 1987. It argues that FDA has misinterpreted the second portion of the exclusionary clause, reading into the "prior market clause" an extra-statutory requirement: that, for a food constitutent to have been "marketed as a dietary supplement or as a food," the manufacturer of the food containing the constitutent must have promoted the food based on the properties of the food constituent at issue, or in some way must have increased or optimized the concentration of the constituent as issue, prior to the constituent's approval as a "new drug."

Pharmanex contends that this interpretation is inconsistent with both the plain language of the statute and FDA's prior interpretation of the term "marketed as," and therefore, *Chevron*

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[4] While the court has determined that all of FDA's findings disputed by Pharmanex are supported by the evidence, the court notes that FDA's conclusion based upon those findings–that Pharmanex was manufacturing and marketing lovastatin–could still be upheld without each and every finding being affirmed.

deference is unwarranted. It urges the court to read the prior market clause to include within the definition of "dietary supplement" any "article" that has been approved as a "new drug" but that was, prior to its approval, sold as a dietary supplement or as a food.

Pharmanex also claims that, to the extent that FDA's findings of fact are not solely based on its misinterpretation of the "prior market clause," and to the extent that FDA actually found that red yeast rice containing lovastatin was not sold in the United States and East Asia prior to the approval of lovastatin as a new drug, FDA's determinations were arbitrary and capricious. Specifically, it argues that FDA's conclusions that (1) the red yeast rice in Cholestin is not traditional red rice and (2) traditional red yeast rice did not and does not contain lovastatin, are arbitrary and capricious.

2. FDA's Arguments

FDA argues that its determination that lovastatin was not marketed as a dietary supplement prior to its approval as a new drug is not arbitrary and capricious.[5] It claims that

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[5] FDA has pointed out and this court agrees that the Tenth Circuit remanded this case for resolution of *record-based* issues, and Pharmanex had not previously made this statutory interpretation argument. Thus, Pharmanex's argument is improper. Nevertheless, the court also agrees with FDA's assertion that, even if this court evaluates FDA's interpretation of the statute on a legal error standard, the statutory language regarding "marketed as" is just as ambiguous as the statutory language that the Tenth Circuit previously found in this case to be entitled to *Chevron* deference. FDA criticizes Pharmanex's argument that "marketed as" means "sold as." Thus, according to Pharmanex, if an article was merely *present* in food, it was marketed as food. Taking Pharmanex's use of the word "sell," which is a synonym for "market," FDA points out that "sell" itself has many meanings. FDA claims that, because "marketed as" is ambiguous, FDA may interpret it to mean more than mere presence. Because its interpretation is reasonable, FDA argues that FDA should be accorded deference under *Chevron*. It also contends that its interpretation is in accord with the dictionary definition of the term and is also consistent with common usage, with respect to both FDA-regulated and non-FDA regulated products.

Thus, even if Pharmanex had raised the issue previously, the court agrees that the statutory language is ambiguous and must be accorded *Chevron* deference. *See Chevron, U.S.A.,*

Pharmanex has failed to show that lovastatin was previously marketed as a dietary supplement, food, or component of a food, and therefore, Cholestin does not qualify as a dietary supplement.

3. Analysis

Having found that, even if it were appropriate to reach the question of whether FDA properly interpreted the "marketed as" language found in § 321(ff)(3)(B), FDA's interpretation merits *Chevron* deference and is a rational interpretation, *see* footnote 5, the only questions remaining are whether FDA's conclusions that (1) the red yeast rice in Cholestin is not traditional red rice, and (2) traditional red yeast rice did not and does not contain lovastatin, are arbitrary and capricious. As discussed above, the court has concluded that FDA's conclusions regarding these issues are supported by the record and, thus, are not arbitrary and capricious.

Accordingly, FDA's conclusion that lovastatin was not marketed as a dietary supplement or as a food prior to 1987 is affirmed.

IV. CONCLUSION

For the foregoing reasons and good cause appearing, IT IS HEREBY ORDERED that Pharmanex's Motion to Hold Unlawful and Set Aside FDA's Decision of May 20, 1998 (docket entries 77 and 111) is DENIED, and FDA's Motion to Affirm Administrative Decision (docket entry 73) is GRANTED, and FDA's Decision of May 20, 1998 is AFFIRMED. Accordingly,

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Inc. v. NRDC, 467 U.S. 837, 842-44 (1984). *United States v. Undetermined Quantities of Bottles*, 22 F.3d 235, 237-38 (10th Cir. 1994). Accordingly, the court finds that FDA's construction of the "marketed as" language to mean more than mere presence in a food is rational and consistent with the statute.

Pharmanex's Complaint is DISMISSED.

DATED this 30th day of March, 2001.

BY THE COURT:

DALE A. KIMBALL
United States District Judge

alt

United States District Court
for the
District of Utah
March 30, 2001

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Re: 2:97-cv-00262

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